Amendments to the Specification

IN THE ABSTRACT OF THE DISCLOSURE

Attached hereto is a replacement Abstract with markings to show amendments.

IN THE WRITTEN DESCRIPTION

Please replace the paragraphs beginning at page 1, line 23, with the following rewritten paragraphs:

Further, solvents for dissolving samples are restricted. A sample having low solubility in the solvents that can be used as the mobile ~~phases~~phase causes a serious problem particularly in chromatographic separation and collection. Moreover, there is another problem in that only limited washing fluids can be used in washing away contaminants strongly adsorbed on the separating agents.

In consideration of those points, a separating agent having a polysaccharide derivative carried thereon and having a high solvent resistance has been strongly required.

In order to solve such problems, there has been proposed a method of imparting solvent resistance to a polysaccharide derivative such as: a method of chemically bonding a polysaccharide derivative to silica gel directly; a method of crosslinking polysaccharide derivatives; and a method combining the above-described methods (JP-A-62-270602, JP-A-04-202141, JP-A-06-329561, JP-A-07-309784, JP-A-07-138301, and JP-A-08-59702).

However, those methods have problems in that a substitution group of the polysaccharide derivative is used for chemical bonding or a crosslinking reaction, thereby causing defects in a regulated structure of the polysaccharide derivative and inhibiting the exhibition of high optical resolving power inherent in the polysaccharide derivative.

DISCLOSURE OF THE INVENTION

It is an object of the present invention to provide a separating agent for enantiomeric isomers capable of exhibiting high optical resolving power inherent in a polysaccharide derivative together with sufficient solvent resistance, and a method of producing the same.

As means for achieving the object, the present invention provides a separating agent for enantiomeric isomers, including a polysaccharide derivative carried on a porous carrier, in ~~which:~~which the porous carrier has an epoxy ~~group;~~group and the epoxy group and part of the hydroxyl groups of the polysaccharide derivative are chemically bonded.

As other means for achieving the object, the present invention provides a method of producing the separating agent for enantiomeric isomers~~ according to any one of claims 1 to 4~~, including the step of chemically bonding a porous carrier having an epoxy group and a polysaccharide derivative having hydroxyl groups by reacting the porous carrier and the polysaccharide derivative in an organic solvent under heating.

As still other means for achieving the object, the present invention provides a method of producing the separating agent for enantiomeric isomers~~ according to any one of claims 1 to 4~~, including the steps of: chemically bonding an epoxy group of a porous carrier and hydroxyl groups of a polysaccharide derivative by reacting the porous carrier having the epoxy group and the polysaccharide derivative having the hydroxyl groups in an organic solvent under heating; and reacting the hydroxyl groups of a product formed in the previous step and a compound having a functional group which may react with the hydroxyl groups.

The present invention relates to ~~a~~the use of a substance, as a separating agent for enantiomeric isomers, which has a polysaccharide derivative carried on a porous carrier, in which: the porous carrier has an epoxy group; and the epoxy group and part of the hydroxyl groups of the polysaccharide derivative are chemically bonded.

The present invention relates to a method of separating enantiomeric isomers by using a substance which has a polysaccharide derivative carried on a porous carrier, in which: the porous carrier has an epoxy group; and the epoxy group and part of hydroxyl groups of the polysaccharide derivative are chemically bonded.

DETAILED DESCRIPTION OF THE INVENTION

A separating agent for enantiomeric isomers according to the present invention includes a polysaccharide derivative carried on a porous carrier through chemical bonding.

A polysaccharide derivative to be used may have an ester bond, a urethane bond, an ether bond, or the like formed by reacting at least part of (but not all) the hydroxyl groups of a polysaccharide with a compound having a functional group capable of reacting with the hydroxyl groups. In particular, the polysaccharide derivative to be used is preferably a polysaccharide carbamate derivative or a polysaccharide ester derivative.

The polysaccharide may be any of a synthetic polysaccharide, a natural polysaccharide, or a modified natural polysaccharide as long as the polysaccharide is optically active. However, the polysaccharide preferably has a highly regulated bonding pattern.

Examples of the polysaccharide include: β-1,4-glucan (cellulose); α-1,4-glucan (amylose or amylopectin); α-1,6-glucan (dextran); β-1,6-glucan (pustulan); β-1,3-glucan (such as curdlan or schizophyllan); α-1,3-glucan; β-1,2-glucan (Crown Gall polysaccharide); β-1,4-galactan; β-1,4-mannan; α-1,6-mannan; β-1,2-fructan (inulin); β-2,6-fructan (levan); β-1,4-xylan; β-1,3-xylan; β-1,4-chitosan; α-1,4-N-acetylchitosan (chitin); pullulan; agarose; alginic acid; and starch containing amylose.

Of those, cellulose, amylose, β-1,4-xylan, β-1, 4-chitosan, chitin, β-1,4-mannan, inulin, curdlan, and the like are preferable because they are easily available high purity

polysaccharides. Cellulose and amylose are particularly preferable.

~~A~~The number-average degree of polymerization of the polysaccharide (average number of pyranose rings or furanose rings in a molecule) is 5 or more, and preferably 10 or more. The number-average degree of polymerization thereof has no upper limit, but is desirably 1,000 or less from a viewpoint of easy handling.

The porous carrier has an epoxy group and may be obtained by introducing an epoxy group into a porous organic carrier or a porous inorganic carrier. The porous carrier is preferably a porous inorganic carrier having an epoxy group incorporated thereinto.

Appropriate examples of the porous organic carrier include polymer substances such as polystyrene, polyacrylamide, and polyacrylate. Appropriate examples of the porous inorganic carrier include silica, alumina, magnesia, glass, kaolin, titanium oxide, a silicate, and hydroxyapatite.

A particularly preferable carrier is silica gel, and silica gel has a particle size of 0.1 μm to 10 μm, preferably 1 μm to 300 μm, more preferably 1 μm to 100 μm, and particularly preferably 1 μm to 75 μm. Silica gel has an average pore size of 10 Å to 100 mm, and preferably 50 Å to 50,000 Å. Silica gel is preferably subjected to surface treatment for eliminating an effect of remaining silanol on its surface, but needs not be subjected to surface treatment at all.

~~A~~The bonding ratio of the polysaccharide derivative is preferably 1 to 50 parts by mass, more preferably 1 to 20 parts by mass, and particularly preferably 1 to 10 parts by mass with respect to 100 parts by mass of the separating agent for enantiomeric isomers. The term "bonding ratio of the polysaccharide derivative" as used herein refers to ~~a~~the ratio of the polysaccharide derivative to the separating agent for enantiomeric isomers.

Please replace the paragraphs beginning at page 9, line 7, with the following rewritten paragraphs:

The separating agent for enantiomeric isomers of the present invention, a stationary phase for chromatography using the same, and a stationary phase for continuous liquid chromatography using the same are suitable for enantiomeric isomers analysis technique involving optical separation of a wide range of chiral compounds at high separation factors in the analysis of drugs, food products, agricultural chemicals, and fragrance materials.

The separating agent for enantiomeric isomers of the present invention includes the porous carrier and the polysaccharide derivative chemically bonded thereto, and thus expands ~~a~~the range of selection of a solvent used as a mobile phase when the separating agent for enantiomeric isomers is used as a stationary phase for chromatography.

Please replace the paragraph beginning at page 17, line 2, with the following rewritten paragraph:

1.14 g of a substance having 20 wt% of polysaccharide derivative 1 carried on the porous carrier 1 was left standing in toluene at 80°C for 3 hours. Then, $BF_3 \cdot Et_2O$ (1 µl) was added thereto. A reaction was carried out for 38 hours, to thereby convert unreacted hydroxyl groups of the derivative and a hydroxyl group formed through ring opening of the epoxy group into phenyl carbamates. The obtained separating agent was collected through a 4G-glass filter and sufficiently washed with pyridine and THF. Then, the separating agent was filled into a column [25 × 0.20 cm (i.d.)] through a slurry method. Note that, a bonding ratio of the polysaccharide derivative (ratio of the polysaccharide derivative to the separating agent for enantiomeric isomers) of the obtained filler was calculated in the same manner as in Example 1.

Please replace the paragraph beginning at page 22, line 2, with the following rewritten paragraph:

The separating agents 4-1 to 4-4 obtained in the Examples and the separating agents 5 and 6 obtained in the Comparative Examples were used, to thereby measure the optical resolving power (separation factor α) of each of the separating agents on the following various racemic modifications by means of HPLC. Table 1 shows the results.